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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/678,961	10/03/2003	Michael R. Slater	341.023US1	7299

21186 7590 03/03/2008
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EXAMINER	
VOGEL, NANCY S	
ART UNIT	PAPER NUMBER
1636	
MAIL DATE	DELIVERY MODE
03/03/2008	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	**Application No.** 10/678,961	**Applicant(s)** SLATER ET AL.
	Examiner NANCY VOGEL	**Art Unit** 1636

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 November 2007*.
2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.
3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,3,4,6,9-13,36,84 and 85* is/are pending in the application.
  4a) Of the above claim(s) _____ is/are withdrawn from consideration.
5)☐ Claim(s) _____ is/are allowed.
6)☒ Claim(s) *1,3,4,6,9-13,36,84 and 85* is/are rejected.
7)☐ Claim(s) _____ is/are objected to.
8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.
10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.
  Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
  Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
  a)☐ All b)☐ Some * c)☐ None of:
    1.☐ Certified copies of the priority documents have been received.
    2.☐ Certified copies of the priority documents have been received in Application No. _____.
    3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
  * See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08)
  Paper No(s)/Mail Date *11/5/07*.
4) ☐ Interview Summary (PTO-413)
  Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 11/5/07 has been entered.

Claims 1, 3, 4, 6, 7, 9, 10-13, 36, 84, 85 are pending in the case.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1, 3, 4, 6, 7, 9, 10, 36, 84, 85 are rejected under 35 U.S.C. 103(a) as being unpatentable over Parrott et al. (6,096,523) in view of Santi et al. (US 2004/0166567).

This rejection is maintained essentially for the reasons made of record in the previous Office action, with slight modification made necessary to applicant's amendments to the claims.

Parrott et al. disclose a method for directional subcloning of DNA fragments comprising providing a first vector comprising a first and second infrequent restriction site, between which a DNA of interest is cloned, wherein restriction of said first and second restriction sites does not generate ends complementary to each other, and providing a second vector comprising a third and fourth enzyme sites, wherein the third restriction enzyme generates single stranded ends complementary to the first site, and a fourth restriction enzyme which generates ends that can be ligated to the ends generated by the second restriction enzyme, which permit the oriented joining of the first linear DNA fragment to the second linear DNA fragment (see col. 5, lines 35- col. 6, line 21; see col. 7, lines 23- col. 8 line 5, in which a shuttle vector having a DNA segment of interest is between a CeuI and a TliI site, and in which the vector is restricted with CeuI and TliI, and then inserted into a docking vector which is cut with CeuI and TliI enzymes). The reference discloses that any two rare restriction sites may be used in the first and the second vector, including different ones (col. 5 lines 28-65; col. 7 lines 24- col. 8 line 5). The reference discloses that any vector known in the art may be used, and that factors affecting vector choice are known in the art, including type of replicon and nature and location of selection marker (col. 6, lines 35-54). The difference between the reference and the instant claim is that a second selectable marker which is distinguished from the first marker is present on the second vector, and the first restriction enzyme generates a 3’ TA overhang.

However, Santi et al. (US 2004/0166567) teach methods for subcloning using two different vectors having different selectable markers, for the selection of a vector construct of interest. The reference discloses a method for directional subcloning of DNA fragments comprising using selectable markers on each of two vectors; a gene of interest is cut from a first vector using restriction enzyme sites on either side of the gene of interest, and this fragment is ligated into a second vector which has been cut at two restriction sites on either side of a selectable marker (see Fig. 3, 5, see page 15 paragraphs 0182-0186). The reference discloses restriction endonuclease which may be used, including PvuI, SgfI, PmeI, PacI, all of which are well known commercially available restriction enzymes, with well known recognition sites, which are well known to be useful in particular combinations due to compatible single stranded overhangs. SgfI leaves a 3' TA end. These manipulations of DNA vectors are routine methods commonly practiced in the art and well known to those of skill in the art.

It would have been obvious to one of skill in the art to have modified the disclosure of Parrott, by including selection markers on both of two starting vectors, and by using any particular restriction enzyme sites, as taught by Santi et al., since both references disclose methods of inserting any DNA fragment of interest from a first vector, into a second vector in a directional manner, using selectable markers and appropriate restriction enzyme recognition sites which yield compatible and/or ligatable ends. One would have been motivated to do so by the desire to select for and/or against the presence of any particular DNA fragment in the final construction, a technique which is well known and routine in the art of DNA manipulation. The construction of desired vectors using restriction enzymes is routine and well known in the art, and virtually any desired construct is routinely made using such well known techniques as directional cloning and subcloning, and selection using selection markers. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Claims 1, 3, 4, 6, 7, 9, 10-13, 36, 84, 85 are rejected under 35 U.S.C. 103(a) as being unpatentable over Parrott et al. (6,096,523) in view of Santi et al. (US 2004/0166567).as applied to claims 1, 3, 4, 6, 7, 9, 10, 36, 84, 85 above, and further in view of Innerarity et al. (US 20010029027).

This rejection is maintained essentially for the reasons made of record in the previous Office action, with slight modification made necessary to applicant's amendments to the claims.

Parrott et al. and Santi et al. are cited for the reasons set forth above.
The difference between the references and the instant claims is that sites for one or more restriction enzymes in the open reading frame are protected by methylation so as to prevent digest, and prior to methylation the flanking sites for the first or second restriction enzyme site are contacted with an oligonucleotide complementary to the flanking restriction enzyme site and RecA. However, Innerarity et al. disclose a method of protecting restriction sites using methylation, protecting other restriction enzyme sites by contact with an oligonucleotide complementary to said enzyme sites and RecA (see paragraph 150). This method of protection of restriction sites using methylation, and protection from methylation by binding an oligonucleotide and RecA to a restriction site,

are well known in the art to be useful for the manipulation and construction of vectors having desired fragments, as disclosed by the reference. It would have been obvious to one of ordinary skill in the art to have combined the teaching of Innerarity et al., which discloses methylation of restriction sites which one does not want restriction cutting to take place at, along with protection of sites which one does want said cutting to take place at using oligonucleotide/RecA binding, and the teachings of Parrott et al. and Santi et al., since all three references disclose methods of constructing vectors of interest using restriction enzymes. One would have been motivated to do so by the desire to cut particular fragments out of a vector, without cutting the fragment internally. Such a cloning/subcloning method is routine in the art and would have been obvious to one of ordinary skill in the art, as evidence by the extensive and routine use of such techniques in the art of biotechnology. Based upon the teachings of the cited references, the high skill of one of ordinary skill in the art, and absent evidence to the contrary, there would have been a reasonable expectation of success to result in the claimed invention.

Applicants arguments filed 11/5/07 have been considered but have not been found convincing.

Applicants have argued that there is “no combination of Parrott et al., Santi et al. or Innearity et al. that teaches, suggests or provides the motivation to prepare, Applicant’s vector set or practice Applicant’s method, which employs vectors each with a recognition site for a restriction enzyme that generates blunt ends and a recognition site for a restriction enzyme that generates a 3’ TA overhang for directional cloning, wherein the recognition site for one of the enzymes that generates a 3'TA overhang occurs infrequently in a particular genome" (page 8). However, for the reasons set forth above, it is maintained that the references when considered together, fairly teach the claimed method. It is noted that the SgfI enzyme, known to be a rare cutter, leaves a 3'TA overhang and is disclosed in the Santi et al. reference, as well as being a well known restriction enzyme available commercially. Therefore the rejection is maintained.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to NANCY VOGEL whose telephone number is (571)272-0780. The examiner can normally be reached on 7:00 - 3:30, Monday - Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Joseph Woitach can be reached on (571) 272-0739. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/NANCY VOGEL/
Primary Examiner, Art Unit 1636

NV
2/16/08